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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,303	07/06/2001	Geert Maertens	2752-52	3515

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,303	MAERTENS ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-70,73,74,76,87-90,95-97 and 102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-70,73,74,76,87-90* is/are rejected.

7)☒ Claim(s) *95-97 and 102* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. 08/612,973.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 68-70, 73-74, 76, 87-90, 95-97 and 102 are pending.

Response to Amendment

This is a response to the amendment filed on 05/03/06. Claims 79, 85 and 86 have been canceled. Claims 68-70, 73-74, 76, 87-90, 95-97 and 102 are pending and considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New ground rejections:

Upon reconsidering the claims, new ground rejections are made on the record.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 68-69, 73, 87 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Ralston et al. (WO 92/08734A1).

3. Ralston et al. teach a method for expressing HCV envelope protein E1, wherein the HCV E1 contain a deletion selected from the region located at aa 170-190, aa 260-290 or aa 330-380; and the expression vector is preferably a vaccinia viral vector. Ralston et al. teach that the recombinant vaccinia vector comprises the HCV envelope protein sequence, which is inherently expressed under the vaccinia viral promoter control and the HCV envelope protein sequence is also inherently operably linked to a 5-terminal ATG codon and a 3'-terminal codon (See pages 9-11 and pages 19-21). The full length HCV E1 ranges from amino acid residue 192-384. If the deleted region is located in the range somewhere in 260-290 and 330-380, but before the 285 or

400, the HCV E1 polypeptide will start before the region 170 or 190 and end at a position within the region between the amino acid residues 260- 290 or 330-380. Therefore, the claims 68-69, 73, 76, 87 and 88 are all anticipated by the cited reference.

4. Claims 76 and 87 are rejected under 35 U.S.C. 102(b) as being anticipated by Hsu et al. (Hepatology, May 1993, Vol. 17, No. 5, pp. 763-771).

5. Hsu et al. disclose a recombinant baculovirus expression vector in particular HCV-Bac 3, encoding nucleic acid sequence that encodes the HCV envelope protein E1 ranging from nucleic acid base 400 to 950 or amino acid residues from about 133 to 316, wherein the glycosylation site(s) at the position 325 is removed inherently at the nucleic acid level. Said vector is a live vector comprising the baculovirus viral promoter as the eukaryotic promoter, which drives the HCV envelope protein to be expressed in Sf9 insect cells (See Fig. 1 and section of MATERIAL AND METHODS in page 764). Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 68-70, 73, 87, 88 and 102 are rejected under 35 U.S.C. 102(e) as being anticipated by Selby et al. (US Patent No. 6,121,020A).

8. Selby et al. teach a method for using a viral vector expression system, such as vaccinia viral expression system to express HCV E1 and/or E2 envelope protein(s) (See lines 52-67 on column 9), so that the DNA sequence encoding the desired E1 and/or E2 polypeptide is transcribed into RNA in the host cells transoformed by said vector containing an expression construction under the control of vaccinia viral promoter inherently. The coding sequence may or may not contain a signal peptide or leader sequence. With the present invention, both the naturally occurring signal peptides or heterologous sequences can be used as a signal peptide sequence. The leader sequences can be removed by the host in post-translational process (See column 10). A number of mammalian cell lines are known available for said vector transformation, such as Hela cell, CHO cells, BHL cells, and COS cells, Hep G2 cell and MDBK cells etc. (See column 10). Selby et al. also disclose that the E1 is expressed as a secreted polypeptide lacking all or portion of its membrane spanning domain (See lines 32-39 of column 2). In particular, the E1 polypeptide is expressed from the beginning with the methionine residue, followed by isoleusine and the amino acid 172 of the HCV polyproptein and continuing to amino acid 330 or various end, such as amino acid residue 340, 350, 360, 370 or 380 (Fig. 5 and lines 32-39 of column 2). Amino acids 173 through 191 corresponded to the C-terminus of core serves as a signal sequence. A mature E1 polypeptide begins at the amino acid 192 following to signal sequence (See Example 1 on column 15 and Fig. 1). Therefore, the claimed invention is anticipated by the cited reference.

9. Claims 68-69, 73, 87 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Ralston et al. (US Patent 5,942,234A).

10. Ralston et al. teach a method for expressing HCV envelope protein E1, wherein the HCV E1 may contain a deletion selected from the region located at aa 170-190, aa 260-290 or aa 330-380 (See column 6); and the expression vector is preferably a vaccinia viral vector (column 7). Ralston et al. teach that the recombinant vaccinia vector comprises the HCV envelope protein sequence, which is inherently expressed under the vaccinia viral promoter control and the HCV envelope protein sequence is also inherently operably linked to a 5-terminal ATG codon and a 3'-terminal codon (See pages 9-11 and pages 19-21). The full length HCV E1 ranges from

amino acid residue 192-384. If the deleted region is located in the range somewhere in 260-290 and 330-380, but before the 285 or 400, the HCV E1 polypeptide will start before the region 170 or 190 and end at a position within the region between the amino acid residues 260- 290 or 330-380. Therefore, the claims 68-69, 73, 76, 87 and 88 are all anticipated by the cited reference.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 68-70, 73, 74, 87-90 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selby et al. (US Patent No. 6,121,020A) in view of the disclosures by Tartaglia et al. (Virol. 1992, Vol. 188 (1), pp. 217-232), Sutter et al.(Proc. Natl. Acad. Sci. USA. 1992, Vol. 89, pp. 10847-10851) and Vanderbroeck et al. (Eur. J. Biochem. 1993, Vol. 217, pp. 45-52).

13. Selby et al. teach a method for using a viral vector expression system, such as vaccinia viral expression system to express HCV E1 and/or E2 envelope protein(s) (See lines 52-67 on column 9), so that the DNA sequence encoding the desired E1 and/or E2 polypeptide is transcribed into RNA in the host cells transoformed by said vector containing an expression construction under the control of vaccinia viral promoter inherently. The coding sequence may or may not contain a signal peptide or leader sequence. With the present invention, both the naturally occurring signal peptides or heterologous sequences can be used as a signal peptide sequence. The leader sequences can be removed by the host in post-translational process (See column 10). A number of mammalian cell lines are known available for said vector transformation, such as Hela cell, CHO cells, BHL cells, and COS cells, Hep G2 cell and MDBK cells etc (See column 10). Selby et al. also disclose that the E1 is expressed as a secreted polypeptide lacking all or portion of its membrane spanning domain (See lines 32-39 of column

2). In particular, the E1 polypeptide is expressed from the beginning with the methionine residue, followed by isoleusine and the amino acid 172 of the HCV polyproptein and continuing to amino acid 330 or various end, such as amino acid residue 340, 350, 360, 370 or 380 (Fig. 5 and lines 32-39 of column 2). Amino acids 173 through 191 corresponded to the C-terminus of core serves as a signal sequence. A Mature E1 polypeptide begins at the amino acid 192 following to signal sequence (See Example 1 on column 15 and Fig. 1). Selby et al. do not teach to use particular vaccinia viral vector, such as Avipox or Ankara Modified virus (AMV) as the vaccinina viral vector to express the particular truncated HCV envelope protein, wherein said truncated HCV E1 is expressed fusion protein that contains the fusion tag of a factor Xa at the 5' terminus and/or preferably 6 histidine codons added as 3' terminus.

14. Targilia et al. teach that the avipox virus canarypox (ALVAC) is a highly attenuated avian species of vaccinia virus strain. It was demonstrated to have the following characteristics: (a) no detectable duration or ulceration at the site of inoculation on rabbit skin; (b) rapid clearance of infectious virus from the intradermal site of inoculation on rabbit skin; (c) absence of testicular inflammation in nude mice; (d) greatly reduced virulence as demonstrated by the results of intracranial challenge of both 3-week-old or newborn mice; (e) greatly reduced pathogenicity and failure to disseminate in immunodeficient (nude or cyclophosphamide treated) mice; and (f) dramatically reduced ability to replicate on a variety of human tissue culture cells. Despite these highly attenuated characteristics, the vector made by NYVAC strain retains the ability to induce strong immune responses to extrinsic antigens (See abstract).

15. Sutter et al. teach that modified vaccina Ankara (MVA), is also a highly attenuated vaccinia virus strain that has been safety tested in human. It is approved that said virus is valuable for use as an efficient and exceptional safe vector for expressing any heterologous gene that it carries (See abstract).

16. Vanderbroeck et al. teach a method about how to use a factor-Xa cleavage site and histidine tag sequence as a fusion tag for expressing a fusion protein by constructing said tag sequences into an expression vector. The fusion protein containing said both or either one of the tags can be more easily identified and efficiently purified by commercial chromolgraphic procedure. Vanderbroeck et al. also disclose to use 6 histidine codones are 6 as fusion tag in the construct inserted at the (See Abstract and Materials and Methods disclosed on pages 45-47).

17. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to combine the method taught by Selby et al., Tartaglia et al. and Sutter et al. in further view of the technique of using the fusion tag disclosed by Vanderbroeck et al. to select the particular vaccinia viral vector and express the HCV envelope protein as a fusion protein containing the fusion tag disclosed by Vanderbroeck et al. in order to get for efficient expression and easily purified fusion protein of HCV E1. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

Claim 95 is free of art rejection. No prior art teaches or suggests to make a vector fro expressing the particular HCV envelope protein cited in claim 95.

Claims 96-97 are objected because though the sequences cited in the claims are not taught or suggested by any prior art, claims 96 and 97 are not in condition for allowance because they depend on the rejected claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bao Qun Li BAOQUN LI, MD PATENT EXAMINER 06/06/2006

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